

WHAT IS CLAIMED IS:

1. An isolated polynucleotide containing the following nucleotide sequence:
- 5 fchd531 (SEQ ID NO.:1),  
fchd540 (SEQ ID NO.:2),  
fchd545 (SEQ ID NO.:3),  
fchd602 (SEQ ID NO.:4) or,  
fchd605 (SEQ ID NO.:5).
- 10 or the nucleotide sequence of a gene or gene fragment contained in the following clone as deposited with the ATCC:  
pFCHD531 (in ATCC Accession No. 69983),  
pFCHD540 (in ATCC Accession No. 69984), or  
fchd545 (in ATCC Accession No. 69974).
- 15 2. An isolated polynucleotide which hybridizes under stringent conditions to the nucleotide sequence of Claim 1 or its complement, or to the gene or gene fragment contained in the clone of Claim 1 as deposited with the ATCC.
- 20 3. An isolated polynucleotide which encodes an amino acid sequence encoded by the nucleotide sequence of Claim 1 or its complement, or encoded by the gene or gene fragment contained in the clone of Claim 1 as deposited with the ATCC.
- 25 4. A polynucleotide vector containing the nucleotide sequence of Claim 1, 2 or 3.
5. A polynucleotide expression vector containing the  
30 nucleotide sequence of Claim 1, 2 or 3 in operative association with a nucleotide regulatory element that controls expression of the nucleotide sequence in a host cell.
- 35 6. A genetically engineered host cell containing the polynucleotide of Claim 1, 2 or 3.

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7. A genetically engineered host cell containing the polynucleotide of Claim 1, 2 or 3 in operative association with a nucleotide regulatory element that controls expression of the nucleotide sequence in the host cell.

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8. A substantially pure gene product encoded by the polynucleotide of Claim 1, 2, or 3.

9. An antibody that immunospecifically binds the gene  
10 product of Claim 8.

10. A transgenic animal in which the polynucleotide of Claim 1, 2 or 3 is an expressed transgene contained in the genome of the animal.

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11. A transgenic animal in which expression of genomic sequences encoding the gene product of Claim 8 is prevented or suppressed.

20 12. A method for diagnosing cardiovascular disease, comprising assaying, in a patient sample, the differential expression of a gene encoding the fchd531 protein, the fchd540 protein, the fchd545 protein, the fchd602 protein, or the fchd605 protein.

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13. The method of Claim 12 in which the cardiovascular disease is atherosclerosis.

14. The method of Claim 12 in which the cardiovascular  
30 disease is ischemia/reperfusion.

15. The method of Claim 12 in which the cardiovascular disease is hypertension.

35 16. The method of Claim 12 in which the cardiovascular disease is restenosis.

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17. The method of Claim 12 in which the gene is up-regulated.

18. The method of Claim 17 in which the gene encodes the  
5 fchd540, fchd602, or fchd605 protein.

19. The method of Claim 12 in which the gene is down-regulated.

10 20. The method of Claim 19 in which the gene encodes the  
fchd531 or fchd545 protein.

21. A method for treating cardiovascular disease,  
comprising administering a compound that modulates the  
15 expression of, or the activity of the encoded protein product  
of, the fchd531 gene, the fchd540 gene, the fchd545 gene, the  
fchd602 gene, or the fchd605 gene to a patient in need of  
such treatment.

20 22. The method of claim 21 in which the cardiovascular  
disease is atherosclerosis.

23. The method of claim 21 in which the cardiovascular  
disease is ischemia/reperfusion.

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24. The method of claim 21 in which the cardiovascular  
disease is hypertension.

25. The method of claim 21 in which the cardiovascular  
30 disease is restenosis.

26. The method of Claim 21 in which the compound inhibits  
the expression of the gene or the activity of the protein  
product.

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27. The method of Claim 26 in which the gene is the  
fchd540, fchd602, or fchd605 gene.

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28. The method of Claim 27 in which the compound is an antisense or ribozyme molecule that blocks translation of the gene.

5 29. The method of Claim 27 in which the compound is complementary to the 5' region of the gene and blocks transcription via triple helix formation.

30. The method of Claim 26 in which the compound is an  
10 antibody that inhibits the activity of the protein product.

31. The method of Claim 21 in which the compound enhances the expression of the gene or the activity the protein product.

15 32. The method of Claim 31 in which the gene is the fchd531 or fchd545 gene.

33. A method for treating cardiovascular disease,  
20 comprising administering a polynucleotide encoding the fchd531 or fchd545 protein to a patient in need of such treatment.

34. A method for treating cardiovascular disease,  
25 comprising administering an effective amount of the fchd531 or fchd545 protein to a patient in need of such therapy.

35. A method for monitoring the efficacy of a compound in clinical trials for the treatment of cardiovascular disease,  
30 comprising assaying, in a patient sample, the differential expression of a gene encoding the fchd531 protein, the fchd540 protein, the fchd545 protein, the fchd602 protein, or the fchd605 protein.

35 36. The method of Claim 35 in which the cardiovascular disease is atherosclerosis.

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37. The method of Claim 35 in which the cardiovascular disease is ischemia/reperfusion.

38. The method of Claim 35 in which the cardiovascular disease is hypertension.

39. The method of Claim 35 in which the cardiovascular disease is restenosis.

40. The method of Claim 35 in which the gene is up-regulated.

41. The method of Claim 40 in which the gene encodes the fchd540, fchd602, or fchd605 protein.

42. The method of Claim 35 in which the gene is down-regulated.

43. The method of Claim 42 in which the gene encodes the fchd531 or fchd545 protein.

44. A method for identifying a substance for treating cardiovascular disease comprising assaying the ability of the substance to modulate the expression of, or the activity of the encoded protein product of, the fchd531 gene, the fchd540 gene, the fchd545 gene, the fchd602 gene, or the fchd605 gene.

45. The method of Claim 44 in which the cardiovascular disease is atherosclerosis.

46. The method of Claim 44 in which the cardiovascular disease is ischemia/reperfusion.

47. The method of Claim 44 in which the cardiovascular disease is hypertension.

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48. The method of Claim 44 in which the cardiovascular disease is restenosis.

49. The method of Claim 44 in which the modulation of  
5 expression of said gene is assayed by:

(a) exposing a sample of cells to a test substance;  
(b) assaying the expression of said gene in the  
sample of cells; and

(c) comparing the expression level of the gene in the  
10 sample exposed to the substance to the expression level of  
the gene in a control sample of cells, in which a difference  
between the expression level of the gene in the sample  
exposed to the substance and the control indicates the  
modulation of expression of the gene.

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50. The method of Claim 49 in which the gene is down-  
regulated by the test substance.

51. The method of Claim 50 in which the substance is an  
20 oligonucleotide complementary to the 5' region of the gene  
and blocks transcription via triple helix formation.

52. The method of Claim 50 in which the substance is an  
antisense or ribozyme molecule that blocks translation of the  
25 gene.

53. The method of Claim 49 in which the gene is up-  
regulated by the test substance.

30 54. The method of claim 44 in which the substance is a  
small organic or inorganic molecule that modulates the  
activity of the protein product by binding to the protein  
product.

35 55. The method of claim 44 in which the substance is an  
antibody that modulates the activity of the protein product  
by binding to the protein product.

56. An assay for identifying a substance that binds to the fchd531 protein, the fchd540 protein, the fchd545 protein, the fchd602 protein, or the fchd605 protein, comprising:

- (a) contacting a protein or peptide containing an amino acid sequence corresponding to the binding site of the protein with a test substance, under conditions and for a time sufficient to permit binding and formation of a complex between the protein or peptide and the test substance, and
- (b) detecting the formation of a complex, in which the ability of the test substance to bind to the protein is indicated by the presence of the test substance in the complex.

57. An assay for identifying a substance that inhibits the interaction between the rchd534 protein and the fchd540 protein comprising:

- (a) contacting a protein or peptide containing an amino acid sequence corresponding to the binding site of the rchd534 protein with a protein or peptide containing an amino acid sequence corresponding to the binding site of the fchd540 protein, under conditions and for a time sufficient to permit binding and formation of a complex, in the presence of a test substance, and
- (b) detecting the formation of a complex, in which the ability of a test substance to inhibit the interaction between the rchd534 protein and fchd540 protein is indicated by a decrease in complex formation as compared to the amount of complex formed in the absence of the test substance.

58. An assay for identifying a substance that inhibits the interaction between two rchd534 protein molecules comprising:

- (a) contacting a first protein or peptide containing an amino acid sequence corresponding to the binding site of the rchd534 protein with a second protein or peptide containing an amino acid sequence corresponding to the binding site of the rchd534 protein, under conditions and for

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a time sufficient to permit binding and formation of a complex, in the presence of a test substance, and

(b) detecting the formation of a complex, in which the ability of a test substance to inhibit the interaction  
5 between two rchd534 protein molecules is indicated by a decrease in complex formation as compared to the amount of complex formed in the absence of the test substance.

59. An assay for identifying a substance that inhibits the  
10 interaction between the rchd534 protein and a protein member of the TGF- $\beta$  signalling pathway comprising:

(a) contacting a protein or peptide containing an amino acid sequence corresponding to the binding site of the rchd534 protein with a protein or peptide containing an amino  
15 acid sequence corresponding to the binding site of the protein member of the TGF- $\beta$  signalling pathway, under conditions and for a time sufficient to permit binding and formation of a complex, in the presence of a test substance, and

20 (b) detecting the formation of a complex, in which the ability of a test substance to inhibit the interaction between the rchd534 protein and the protein member of the TGF- $\beta$  signalling pathway is indicated by a decrease in complex formation as compared to the amount of complex formed  
25 in the absence of the test substance.

60. The assay of Claim 59 wherein the protein member of the TGF- $\beta$  signalling pathway is MADR1, MADR2, DPC4, activated T $\beta$ R1, activated ActR1b, or activated ALK6.

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61. An assay for identifying a substance that inhibits the interaction between the fchd540 protein and a protein member of the TGF- $\beta$  signalling pathway comprising:

(a) contacting a protein or peptide containing an  
35 amino acid sequence corresponding to the binding site of the fchd540 protein with a protein or peptide containing an amino acid sequence corresponding to the binding site of the



protein member of the TGF- $\beta$  signalling pathway, under conditions and for a time sufficient to permit binding and formation of a complex, in the presence of a test substance, and

- 5 (b) detecting the formation of a complex, in which the ability of the test substance to inhibit the interaction between the fchd540 protein and the protein member of the TGF- $\beta$  signalling pathway is indicated by a decrease in complex formation as compared to the amount of complex formed  
10 in the absence of the test substance.

62. The assay of Claim 61 wherein the protein member of the TGF- $\beta$  signalling pathway is MADR1, MADR2, DPC4, activated T $\beta$ R1, activated ALK6, activated TSR1, activated ALK3, or  
15 activated ActR1 $\beta$ .

63. A method for treating cardiovascular disease comprising administering a compound that inhibits the interaction between the rchd534 protein and the fchd540  
20 protein.

64. A method for treating cardiovascular disease comprising administering a compound that inhibits the interaction between two rchd534 protein molecules.  
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65. A method for treating cardiovascular disease comprising administering a compound that inhibits the interaction between the rchd534 protein and a protein member of the TGF- $\beta$  signalling pathway.  
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66. The method of Claim 65 wherein the protein member of the TGF- $\beta$  signalling pathway is MADR1, MADR2, DPC4, activated T $\beta$ R1, activated ActR1b, or activated ALK6.

35 67. A method for treating cardiovascular disease comprising administering a compound that inhibits the

interaction between the fchd540 protein and a protein member of the TGF- $\beta$  signalling pathway.

68. The method of Claim 67 wherein the protein member of  
5 the TGF- $\beta$  signalling pathway is MADR1, MADR2, DPC4, activated T $\beta$ R1, activated ALK6, activated TSR1, activated ALK3, or activated ActR1 $\beta$ .

69. A method for identifying a substance that enhances the  
10 TGF- $\beta$  signalling response comprising:

(a) contacting a genetically engineered cell with a test substance, said cell comprising 1) a reporter gene in operative association with an inducible TGF- $\beta$  regulatory element; 2) a recombinant gene encoding the rchd534 protein  
15 or a recombinant gene encoding the fchd540 protein; and 3) a recombinant gene encoding the MADR1 protein or a recombinant gene encoding the MADR2 protein; and

(b) detecting expression of said reporter gene in which ability of the test substance to enhance the TGF- $\beta$  signalling  
20 response is indicated by an increase in expression of the reporter gene as compared to the amount of expression in the absence of the test substance.

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